

What is claimed is:

1. A method for modulating tumor growth or
5 metastasis in an animal in need thereof, comprising
sequential or simultaneous administration of at least
one anticancer agent, and a combretastatin A-4 compound
in amounts effective therefore.
- 10 *2.* A method for modulating tumor growth or
metastasis in an animal in need thereof, comprising
administration of a combretastatin A-4 compound and at
least one anticancer agent, in amounts effective
therefor, wherein said combretastatin A-4 compound is
15 administered at a time relative to administration of
said anticancer agent sufficient to modulate blood flow
to said tumor to provide a time-dependent effective
tumor concentration of said anticancer agent.
- 20 3. The method as claimed in claim 1, wherein said
at least one anti-cancer agent is selected from the
group consisting of alkylating agents, bifunctional
alkylating agents, non-steroidal aromatase inhibitors,
immunotherapeutic agents, nitrosurea compounds,
25 antimetabolites, antitumor antibiotics, mitotic
inhibitors, radiation, topoisomerase I inhibitors, and
anti-estrogens.
- 30 4. The method as claimed in claim 1, wherein said
at least one anticancer agent is selected from the group
consisting of cisplatin, carboplatin, oxaliplatin,
radiation, CPT-11, paclitaxel, 5-flourouracil,
leucovorin, epothilone, gemcitabine, UFT, herceptin,
cytoxan, dacarbazine, ifosfamide, mechlorethamine,

melphalan, chlorambucil, anastrozole and exemstane, carmustine, lomustine, methotrexate, gemcitabine, cytarabine, fludarabine, bleomycin, dactinomycin, daunorubicin, doxorubicin, idarubicin, docetaxel,

5 vinblastine, vincristin, vinorelbine, topotecan, lupron, megace, leucovorin, Iressa, flavopiridol, immunotherapeutic agents, ZD6474, SU6668, and valsphospar.

10 5. The method as claimed in claim 2, wherein said anti-cancer agent is a "peak tumor concentration agent" and is administered simultaneously or close temporal proximity to said combretastatin A4 compound.

15 6. The method as claimed in claim 5, wherein said peak tumor concentration agent is selected from the group consisting of cytoxin, mitomycin C, cisplatin, oxaliplatin, and carboplatin.

20 7. The method as claimed in claim 2 wherein said anticancer agent is a duration exposure agent and is administered after the administration of the combretastatin A4 compound.

25 8. The method as claimed in claim 7, wherein said duration exposure agent is selected from the group consisting of taxanes, etoposide, etoposide phosphate, immunotoxins and epothilones.

30 9. The method as claimed in claim 2, wherein said anti-cancer agent is an AUC agent and said AUC agent is administered prior to the administration of said combretastatin A4 compound.

10. The method as claimed in claim 9, wherein said AUC agent is selected from the group consisting of adriamycin, CTP-11 and topotecan.

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11. The method as claimed in claim 6, wherein said combretastatin A4 compound is combretastatin A-4 phosphate disodium salt and said peak tumor concentration agent is cisplatin.

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12. The method as claimed in claim 6, wherein said combretastatin A4 compound is combretastatin A-4 phosphate disodium salt and said peak tumor concentration agent is carboplatin.

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13. The method as claimed in claim 10, wherein said combretastatin A4 compound is combretastatin A-4 disodium salt and said AUC agent is CPT-11.

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14. The method as claimed in claim 8, wherein said combretastatin A4 compound is combretastain A-4 disodium salt and said duration exposure agent is paclitaxel.

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15. The method as claimed in claim 14, wherein said combretastatin A4 disodium salt is administered at least 3 hours prior to paclitaxel.

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16. A method for modulating tumor growth or metastasis in an animal in need thereof, comprising sequential or simultaneous administration of at least one anticancer agent, and a combretastatin A-1 compound in amounts effective therefore.

17. A method for modulating tumor growth or metastasis in an animal in need thereof, comprising administration of a combretastatin A-1 compound and at least one anticancer agent, in amounts effective
5 therefor, wherein said combretastatin A-1 compound is administered at a time relative to administration of said anticancer agent sufficient to modulate blood flow to said tumor to provide a time-dependent effective tumor concentration of said anticancer agent.

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18. The method as claimed in claim 16, wherein said at least one anticancer agent is selected from the group consisting of cisplatin, carboplatin, oxaliplatin, radiation, CPT-11, paclitaxel, 5-flourouracil,
15 leucovorin, epothilone, gemcitabine, UFT, herceptin, cytoxan, dacarbazine, ifosfamide, mechlorethamine, melphalan, chlorambucil, anastrozole, exemestane, carmustine, lomustine, methotrexate, mitomycin C, gemcitabine, cytarabine, fludarabine, bleomycin,
20 dactinomycin, daunorubicin, doxorubicin, idarubicin, docetaxel, vinblastine, vincristine, vinorelbine, topotecan, lupron, megace, leucovorin, Iressa, flavopiridol, an immunotherapeutic agent, ZD6474, SU6668, and valspar.

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19. The method as claimed in claim 17, wherein said combretastatin A-1 compound is combretastatin A-1 disodium salt and said anti-cancer agent is carboplatin.

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20. The method as claimed in claim 17, wherein said combretastatin A-1 compound is combretastatin A-1 disodium salt and said anti-cancer agent is cisplatin.

21. The method as claimed in claim 17, wherein said combretastatin A-1 compound is combretastatin A-1 disodium salt and said immunotherapeutic agent is BR96-sfv-PE40.

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22. A pharmaceutical composition for modulating tumor growth or metastasis in an animal in need thereof, comprising at least one anticancer agent, and a combretastatin A-4 compound, in amounts effective therefore in a pharmaceutically acceptable carrier.

23. The pharmaceutical composition as claimed in claim 22, wherein said at least one anticancer agent is selected from the group consisting of cisplatin, carboplatin, oxaliplatin, radiation, CPT-11, paclitaxel, 5-flourouracil, leucovorin, epothilone, gemcitabine, UFT, herceptin, cytoxan, dacarbazine, ifosfamide, mechlorethamine, melphalan, chlorambucil, anastrozole and exemstane, carmustine, lomustine, methotrexate, gemcitabine, cytarabine, mitomycin C, fludarabine, bleomycin, dactinomycin, daunorubicin, doxorubicin, idarubicin, docetaxel, vinblastine, vincristin, vinorelbine, topotecan, lupron, megace, leucovorin, Iressa, flavopiridol, an immunotherapeutic agent, ZD6474, SU6668, and valspar.

24. The pharmaceutical composition of claim 23, wherein said combretastatin A-4 compound is combretastain A-4 disodium salt.

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25. The pharmaceutical composition as claimed in claim 23, wherein said at least one anti-cancer agent is selected from the group consisting of cytoxan, mitomycin

C, cisplatin, oxaliplatin, and carboplatin.

26. The pharmaceutical composition as claimed in
claim 24, wherein said at least one anti-cancer agent is
5 selected from the group consisting of cytoxan, mitomycin
C, cisplatin, oxaliplatin, and carboplatin.

27. The pharmaceutical composition as claimed in
claim 23, wherein said at least one anticancer agent is
10 selected from the group consisting of taxanes,
paclitaxel, docetaxel, etoposide, etoposide phosphate,
and epothilones.

28. The pharmaceutical composition as claimed in
15 claim 24, wherein said at least one anticancer agent is
selected from the group consisting of taxanes,
paclitaxel, docetaxel, etoposide, etoposide phosphate,
and epothilones.

20 29. The pharmaceutical composition as claimed in
claim 23, wherein said at least one anti-cancer agent is
selected from the group consisting of adriamycin, CTP-11
and topotecan.

25 30. The pharmaceutical composition as claimed in
claim 24, wherein said at least one anti-cancer agent is
selected from the group consisting of adriamycin, CTP-11
and topotecan.

30 31. The pharmaceutical composition as claimed in
claim 23, wherein said anti-cancer agent is cisplatin.

32. The pharmaceutical composition as claimed in

claim 24, wherein said anti-cancer agent is cisplatin.

33. The pharmaceutical composition as claimed in
claim 23, wherein said anti-cancer agent is carboplatin.

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34. The pharmaceutical composition as claimed in
claim 24, wherein said anti-cancer agent is carboplatin.

10 35. The pharmaceutical composition as claimed in
claim 23, wherein said anti-cancer agent is CPT-11.

36. The pharmaceutical composition as claimed in
claim 24, wherein said anti-cancer agent is CPT-11.

15 37. The pharmaceutical composition as claimed in
claim 23, wherein said anti-cancer agent is paclitaxel.

39. The pharmaceutical composition as claimed in
claim 24, wherein said anti-cancer agent is paclitaxel.

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40. The pharmaceutical composition as claimed in
claim 23, wherein said immunotherapeutic agent is BR96-
sfv-PE40.

25 41. The pharmaceutical composition as claimed in
claim 24, wherein said immunotherapeutic agent is BR96-
sfv-PE40.

30 42. A pharmaceutical composition for modulating
tumor growth or metastasis in an animal in need thereof,
comprising at least one anticancer agent, and a
comberstatin A-1 compound, in amounts effective
therefore in a pharmaceutically acceptable carrier.

43. The pharmaceutical composition as claimed in
claim 42, wherein said at least one anticancer agent is
selected from the group consisting of cisplatin,
5 carboplatin, oxaliplatin, radiation, CPT-11, 5-
flourouracil, leucovorin, epothilone, gemcitabine, UFT,
herceptin, cytoxan, taxanes, dacarbazine, ifosfamide,
mechlorethamine, melphalan, chlorambucil, anastrozole
and exemstane, carmustine, lomustine, methotrexate,
10 gemcitabine, cytarabine, fludarabine, bleomycin,
dactinomycin, daunorubicin, doxorubicin, idarubicin,
docetaxel, vinblastine, vincristin, vinorelbine,
topotecan, lupron, megace, leucovorin, Iressa, mitomycin
C, flavopiridol, ZD6474, SU6668, an immunotherapeutic
15 agent and valspar.

44. The pharmaceutical composition of claim 43,
wherein said combretastatin A-1 compound is
combreastatin A-1 disodium salt.

20 45. The pharmaceutical composition as claimed in
claim 43, wherein said at least one anti-cancer agent is
selected from the group consisting of cytoxan, mitomycin
C, cisplatin, oxaliplatin, and carboplatin.

25 46. The pharmaceutical composition as claimed in
claim 44, wherein said at least one anti-cancer agent is
selected from the group consisting of cytoxan, mitomycin
C, cisplatin, oxaliplatin, and carboplatin.

30 47. The pharmaceutical composition as claimed in
claim 43, wherein said at least one anticancer agent is
selected from the group consisting of taxanes,

etoposide, etoposide phosphate, and epothilones.

48. The pharmaceutical composition as claimed in
claim 44, wherein said at least one anticancer agent is
5 selected from the group consisting of taxanes,
etoposide, etoposide phosphate, and epothilones.

49. The pharmaceutical composition as claimed in
claim 43, wherein said at least one anti-cancer agent is
10 selected from the group consisting of adriamycin, CTP-11
and topotecan.

50. The pharmaceutical composition as claimed in
claim 44, wherein said at least one anti-cancer agent is
15 selected from the group consisting of adriamycin, CTP-11
and topotecan.

51. The pharmaceutical composition as claimed in
claim 43, wherein said anti-cancer agent is cisplatin.
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52. The pharmaceutical composition as claimed in
claim 44, wherein said anti-cancer agent is cisplatin.

53. The pharmaceutical composition as claimed in
25 claim 43, wherein said anti-cancer agent is carboplatin.

54. The pharmaceutical composition as claimed in
claim 44, wherein said anti-cancer agent is carboplatin.

30 55. The pharmaceutical composition as claimed in
claim 43, wherein said anti-cancer agent is CPT-11.

56. The pharmaceutical composition as claimed in

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claim 44, wherein said anti-cancer agent is CPT-11.

57. The pharmaceutical composition as claimed in
claim 43, wherein said anti-cancer agent is paclitaxel.

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58. The pharmaceutical composition as claimed in
claim 44, wherein said anti-cancer agent is paclitaxel.

59. The pharmaceutical composition as claimed in
10 claim 43, wherein said anti-cancer agent is BR96-sfv-
PE40. —

60. The pharmaceutical composition as claimed in
claim 44, wherein said anti-cancer agent is BR96-sfv-
15 PE40. —

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